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ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: NON-INVASIVE METHOD FOR MEASURING RATES OF BIOSYNTHESIS OF BIOLOGICAL MOLECULES BY LABEL INCORPORATION

(57) Abstract: Methods of determining rate of biosynthesis or breakdown of biological molecules from metabolic derivatives and catabolic products are disclosed herein. In particular, methods of measuring the rates of biosynthesis and breakdown of biological molecules inaccessible or not easily accessible to direct sampling by sampling metabolic derivatives and catabolic products in accessible biological samples are disclosed herein.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/04183

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/00
US CL : 435/4, 6, 29

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/4, 6, 29

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	6,1010,846 A (HELLERSTEIN) 04 January 2000 (04.01.2000), especially abstract, columns 3 - 5, 8 - 14	1 - 45, 58-59
A	HELLERSTEIN, MK et al, Mass Isotopomer distribution analysis: a technique for measuring biosynthesis and turnover of polymers, American Journal of Physiology, November 1992, Vol.263 (Pt 1):E900 - 1001, abstract	2,58-59



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

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Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/04183

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1 - 45, 58 - 59

Remark on Protest

☐
☐

- The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/04183

Continuation of Item 4 of the first sheet:

The title is too long. The title has been change to read the following.

Non-invasive Method for Measuring Rates of Biosynthesis of Biological Molecules By Label Incorporation

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1 - 45 and 58 - 59, drawn to a method for determining a rate of biosynthesis.

Group II, claim(s) 46 - 48, drawn to a method to identify a disease sate.

Group III, claim(s) 49 - 52, drawn to a method for monitoring response of a disease.

Group IV, claim(s) 53, drawn to a method for determining the pool size of a biological molecule.

Group V, claim(s) 54 - 57, drawn to a kit.

Regarding Group I, Applicant is allowed a single sequence per invention. As such, each sequence will be treated a separate invention, with only the first named sequence included in Group I. There Applicant is required to elect a sequence relative to claims 24 and 59. If Applicant wishes additional sequences to be searched, the appropriate additional examination fees must be paid.

The inventions listed as Groups I - V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The inventions of each group are drawn to various methods which may be practiced independently of each other. Furthermore, there is not a special technical feature which contributes over the prior art.

Continuation of B. FIELDS SEARCHED Item 3:

WEST, STN-CAS, PubMed

search terms: assay, decomposition, breakdown, biosynthesis, collagen, isotopic label, MIDA, metabolite